ABSTRACTS – POSTER

1028 New Studies Using Platelet Receptor Antagonists

Monday, March 30, 1998, Noon–2:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 1:00 p.m.–2:00 p.m.

1028-107 Thrombocytopenia in a Large, International Trial of the GP IIb/IIIa Inhibitor Eptifibatide in Patients With Acute Coronary Syndromes

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Background: Platelet (plt) inhibition via GP IIb/IIIa receptor blockade is associated with a low but potentially important incidence of thrombocytopenia (T). We sought to examine the incidence of T in PURSUIT, a multicenter international clinical trial studying this mode of platelet inhibition.

Methods: 10,948 patients with a non-ST elevation acute coronary syndrome for <24 hours were randomized to treatment with eptifibatide, a platelet GP IIb/IIIa receptor antagonist, or placebo for up to 96 hours. Patients received aspirin and heparin. T was defined as acute (plt <50% of baseline or <100,000/mm^3), severe (plt <50,000 mm^3), or profound (plt <20,000/mm^3).

Results:

	Overall (n = 10,849)	Eptifibatide (n = 4,679)	Placebo (n = 4,696)
Acute T	6.9%	6.8%	6.7%
Severe T	0.5%	0.6%	0.4%
Profound	0.1%	0.2%	0.0%

Conclusion: T occurs infrequently but not rarely among patients with non-ST elevation acute coronary syndromes. The overall incidence of T was similar between treatment groups, with a slight excess of severe and profound T associated with eptifibatide. The clinical significance of T in this population remains to be determined.

1028-108 Prior Aspirin use Potentiates the Effect of GP IIb/IIIa Inhibition in Patients With Non-ST Elevation Acute Coronary Syndromes

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Background: Aspirin (ASA) is the most commonly used anti-platelet agent in pts with coronary artery disease. The additional benefit of GP IIb/IIIa inhibition during an acute coronary event in pts already on ASA is unknown.

Methods: The PURSUIT trial randomized 10,948 pts with non-ST elevation acute coronary syndromes to bolus and infusion of eptifibatide or placebo for up to 72 hours. Pts were followed for 30d death or non-fatal MI. Protocol ASA use (160 mg then 75–325 mg/d) was recommended in all pts. We studied the relationship between prior ASA use (within 2 weeks) and treatment effect of eptifibatide.

Results: Overall, prior ASA use was 63.6% and did not vary across treatment arms. Death or MI by ASA use and treatment is displayed:

	Placebo	Eptifibatide	RR	95% CI
No prior aspirin	12.9%	13.1%	1.02	(0.84, 1.25)
Prior aspirin*	17.3%	14.9%	0.84	(0.73, 0.96)

Conclusions: Pts with prior ASA use derived particular benefit from GP IIb/IIIa inhibition. While this counters the expectation that there would be less potential therapeutic effect in patients with prior antiplatelet use, the mechanism of ASA resistance may be explanatory and deserves further study.

1028-109 Comparison of Receptor Occupancy and Platelet Aggregation Response of Eptifibatide Administered Intravenously in Patients With Unstable Angina or Non-Q-Wave Myocardial Infarction

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Background: Eptifibatide is a platelet fibrinogen receptor antagonist suitable for IV administration. PERIGEE is a substudy of PURSUIT, a multicenter, randomized placebo-controlled trial in patients with unstable angina or suspected MI without ST segment elevation.

Methods: A placebo group and a treatment regimen of a 180 μg/kg bolus followed by a 2.0 μg/kg/min infusion rate up to 72 hr were investigated. An objective was to determine the concentration-response curve of eptifibatide vs. placebo for ex vivo platelet aggregation (PA) and platelet GPIIb-IIIa receptor occupancy (RO). The extent RO was determined by the binding of the D3 mAb which measures the percent of total GPIIb-IIIa receptors with bound drug. Both PA and RO were carried out before eptifibatide was administered, at timepoints after drug initiation, prior to drug discontinuation, and at 4 hr and 8 hr after discontinuation.

Results: More than 80% of patients achieved 80% inhibition of PA to 20 μM ADP immediately after the IV bolus and under steady state conditions. Platelet inhibition was rapidly reversible with PA returning to baseline within 4–8 hr after discontinuation of infusion. The RO results temporally paralleled the profile of inhibition of PA. 45% of the patients achieved 80% RO after the IV bolus and more than 65% achieved 80% RO under steady state conditions. A RO of less than 60% was measured at 8 hr after discontinuation of infusion. Furthermore, PK data proved a strong relationship between eptifibatide plasma concentrations and RO.

Conclusions: Eptifibatide caused a concentration dependent effect on RO that mirrored the observed inhibition of PA. RO has advantages in that a pre-drug sample is not required and assessment can be carried out up to 72 hrs post blood collection. RO is an excellent alternative method for monitoring receptor blockade.

1028-110 Dose Ranging Study of Intravenous RPR 109891 in Patients With Acute Coronary Syndromes – Results of TIMI 15A

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Platelet glycoprotein IIb/IIIa receptor blockade is beneficial in high-risk unstable angina and angioplasty. RPR 109891 is a unique competitive inhibitor because it is available in both IV and oral formulations. To study the dose response of the IV formulation, TIMI 15A is randomizing patients with acute coronary syndromes to receive IV RPR 109891 for 24–96 hours. The primary endpoint is inhibition of platelet aggregation (IPA) using ADP-20 μM. Mean IPA at 20 minutes, pre-stop and 2–4 hrs post stop are shown below for 5